

Be on the Lookout for Kratom!

What is Kratom?

Kratom is a complex herbal product that has grown in popularity in the United States (US) over the past 3 decades. It contains 40+ alkaloids derived from leaves of the *Mitragyna speciosa* tree (related to the coffee plant). Its 2 main alkaloids, mitragynine (MG) and 7-hydroxymitragynine (7-OHMG), are primarily mu-opioid receptor agonists similar to opioids that result in analgesia and euphoria. **Opioid-like effects have been reported at moderate to higher doses and stimulant-like effects at lower doses.** Users of kratom often report multiple reasons for use, including to: relax, self-manage pain, increase alertness, increase physical energy, self-treat symptoms of mental health conditions (e.g., anxiety, depression), self-manage drug cravings and withdrawal symptoms from opioid or other substance use, and reduce or stop substance use. It is also perceived by some as a “safer” or “legal” way to get high as opposed to using illicit drugs. Chewing natural leaves and brewing it into tea for stimulant and analgesic effects is the centuries old traditional use of kratom in Southeast Asia. **Many US products are more highly processed and at risk of adulteration and unknown safety issues.** The Food and Drug Administration (FDA) warns consumers about variability in kratom formulations, risks for adulteration, many potential drug interactions, and recommends not to use kratom until there is more use and safety data. There are no FDA approved uses. It is currently listed by the Drug Enforcement Administration (DEA) as a “drug of concern” while it is actively being studied for use and safety.

Is Kratom Legal?

Currently, it is legal in the US but not legal in all states or municipalities. **South Carolina has introduced a bill to add kratom as a Schedule IV controlled substance** and North Carolina has a bill pending to regulate the quality and safety of kratom production, distribution, and sales. Georgia restricts use to ages 18 and older with legislation pending to ban it completely.

What are the Products and Availability?

Kratom goes by many generic names (e.g., biak-biak, cratom, gratom, ithang, kakuam, katawn, kedemba, ketum, krathom, kraton, kratum, madat, maeng da leaf, mambog, mitragynine, mitragynine extract, thang, thom). The number of US vendors has expanded and products include capsules, powders, extracts, tinctures, gummies, resins, smoking/vaping formulations, and raw powder. **Americans often buy more concentrated oral formulations.** Many people buy kratom on the Internet and it can also be found in gas stations, specialty herb shops, smoke/vape shops, “legal high” shops, or kratom bars.

What are Product Safety Concerns?

Product formulations and effects vary widely. Product potency is affected by many factors, including agricultural variations in plant material and a lack of FDA approved manufacturing standards. Like all dietary supplements without standards, **there is also an increased risk of adulteration** with other constituents such as illegal drugs, bacteria (e.g., Salmonella), or heavy metals (e.g., lead). Adulterated products found fortified with 7-OHMG (up to 6 times more than naturally found in raw leaves) are concerning as 7-OHMG has been reported at least 10 times more potent than morphine in activating mu-opioid receptors.

What are Other Safety Concerns?

Adverse effects and drug interactions

Adverse effects range from mild to severe; reported deaths are rare compared to deaths from other drugs. The most commonly reported adverse effects in US adults include dizziness, drowsiness, nausea, vomiting, constipation, headache, agitation or irritability, tachycardia, hypertension, confusion, and seizures in patients with and without seizure disorders. Life-threatening adverse effects are rarely reported and include coma, cardiac arrest, respiratory arrest, and renal failure. Liver impairment of unpredictable onset and severity has also been reported. Of note, over half of the 300 kratom-associated deaths reported worldwide through 2019 occurred in the US, with up to 95% of cases reporting presence of other drugs (e.g., opioids, stimulants, alcohol, benzodiazepines). There is the potential for multiple kratom-drug interactions beyond additive CNS depression, including interactions with drugs metabolized by the cytochrome P450 system.

Intoxication and overdose

Acute overdose symptoms commonly reported are stimulant-like (e.g., tachycardia, agitation, hypertension, vomiting, and seizures) or opioid-like effects (e.g., confusion, somnolence, obtundation, and rarely, respiratory depression). There are no treatment guidelines and management includes stopping kratom use and providing symptomatic care. Respiratory status and seizure activity should be carefully assessed; naloxone treatment has been reported to be successful in reversing respiratory depression, but not in all cases.

Dependence, withdrawal, and addiction

Physical dependence (linked to high-dose and frequency >3 times per day ≥6 months) and opioid-like withdrawal symptoms have been reported as well as tolerance and opioid cross tolerance. Withdrawal typically begins within 24 hours after the last dose. It has been described as generally milder and of less duration than opioids. Mild withdrawal effects have been reported to be managed with just a gradual kratom taper. With no current guidelines, more severe or long-lasting withdrawal symptoms have generally been managed similar to opioid withdrawal symptoms. There are multiple cases of Neonatal Abstinence Syndrome due to maternal kratom use, including women regularly using kratom but not opioids. These newborns are managed similarly to those with Neonatal Opioid Withdrawal Syndrome (NOWS). Kratom users can develop “kratom use disorder” (KUD). In a small survey of addiction medicine physicians, 4 out of 5 reported cases they considered KUD. KUD has been managed with medications for opioid use disorder (OUD) in some cases; there is debate about using buprenorphine or methadone in those with KUD and no previous OUD.

How Do I Determine Kratom Use by a Patient?

Patient inquiry is key. Kratom cannot be detected by point-of-care/standard drug and toxicology testing and use is often not reported (there is a specialized test available with slow result turn around). **Asking in a respectful and non-judgmental fashion about supplement use, including kratom, as part of a routine medical or mental health evaluation can encourage an honest conversation with your patient. You may have a patient using kratom for recreational purposes; the more likely intent is to self-treat** pain, mental health symptoms, substance use disorders, or withdrawal symptoms. The presence of opioid-like symptoms and a negative drug screen for opioids suggests the need to rule out kratom use. The same would be true for stimulant-like effects with a negative drug screen for stimulants. Survey results suggest adult males are more likely to use kratom; other demographics vary among surveys.

References for this tipSC NOTES and additional tipSC information are available at <https://shealthviz.sc.edu/tipsc-1/> tipSC. Safety and efficacy of Kratom has not been proved for any medical use/condition. Current data about kratom is primarily based on traditional use, self-reporting, and case reports.

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